UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,635	02/20/2004	Ann Marie Schmidt	56613-A JPW/AJM/AAB	1285

7590 07/18/2008

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,635	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49,58-62,65-67,69-73,77 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49,58-62,65-67,69-73,77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The finality of the last Office action is withdrawn, and new grounds of rejection are set forth below.

Response to Amendment

Claim 49 has been amended and claims 64 and 76 have been canceled as requested in the amendment filed on 24 March 2008. Following the amendment, claims 49, 58-62, 65-67, 69-73, 77 and 78 are pending in the instant application.

Claims 49, 58-62, 65-67, 69-73, 77 and 78 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49, 58-62, 65-67, 69-73, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims are directed to a method for treating a subject suffering from kidney failure or amyloidoses, which comprises administering to the subject an amount of quinine or quinidine effective to inhibit the interaction between the AGE and RAGE in the subject, so as to thereby treat the subject.

The specification teaches *in vitro* testing to determine which synthetic AGE structures interact with RAGE. It is taught that CML-modified BSA (not free CML), but not pentosidine or methylglyoxal-modified forms of proteins, bound RAGE in a dose-dependent manner. It is taught that CML-modified forms of proteins increased cell surface VCAM-1 functional activity on human umbilical vein endothelial cells (HUVECs) and increased migration of human peripheral blood-derived mononuclear phagocytes (MPs) in a RAGE-dependent manner. The specification teaches that CML- and RAGE epitopes were increased and co-localized in the kidney tissue from humans with diabetes and that CML content is increased with aging in the serum of diabetic patients and in skin, lung, heart, liver, kidney, intestine, intervertebral discs and arteries. It is taught that other products of peroxidation, glycoxylation and glycation are present in diabetic kidney (pp.28-29). The specification also teaches that quinine and quinidine

are compounds capable of inhibiting the interaction of AGE and RAGE *in vitro* (pp.38-39). The specification does not disclose any examples demonstrating performance of the claimed methods in any specific disease state.

Accordingly, it is well known in the art that successful treatment of amyloidoses, such as Alzheimer's disease, has eluded researches and is therefore quite unpredictable. Alzheimer's disease involves an initial loss of recent memory function and attention, followed by failure of language skills, visual-spatial orientation, abstract thinking, and judgment and alterations of personality (Purves et al; Eds, Neuroscience, 2001, Sinauer Associates, Inc., 2nd Edition, p. 678). The histopathology involves collections of neurofibrillary tangles and senile plaques and diffuse loss of neurons. Applicants have not shown any correlation between the *in vitro* data disclosed in the specification and alleviation of any of the above-mentioned pathologies associated with Alzheimer's disease. No actual therapeutic data is disclosed from human patients or from an art-accepted animal model for Alzheimer's disease (AD) or other amyloidoses. Applicants have not shown that quinine or quinidine would lower plaque burden (for example) in an animal model of AD. However, even if this art accepted model system was used in the instant specification, (i.e., mice that are transgenic for PDAPP and exhibit Alzheimer's type over production and build up of β-amyloid within the brain), this system is still not recognized as providing the teachings that are predictive of the results expected for the claims (treatment of amyloidoses, including AD). Furthermore, the art teaches that there is no known cure, treatment or preventative measure for Alzheimer's disease and related diseases, as evidenced by Vickers (Drugs Aging. 2002; 19(7): 487-

94) who teaches, “Alzheimer's disease (AD) is the leading cause of age-related dementia and is set to markedly increase in incidence with the gradual aging of the populations in both developed and developing nations. Along with most brain diseases and conditions, there is no effective treatment currently available to reverse, slow down or prevent its course."

Regarding the claimed treatment of kidney failure comprising administration of quinine or quinidine, the art teaches that quinine ingestion has a causal association with kidney failure (Maguire et al. Hemolytic anemia and acute renal failure associated with temafloxacin-dependent antibodies. Am J Hematol. 1994 Aug;46(4):363-6, abstract). Thus, if quinine can induce kidney failure, then the disease is not treated. Since treatment of kidney failure is required by the claims, it would require undue experimentation to practice the claimed invention, because the invention would not work as evidenced by the prior art. The specification does not provide guidance to overcome the unpredictability of practicing the claimed invention, since Applicants do not disclose any actual examples of quinine or quinidine used to successfully treat kidney failure in humans or in an art-accepted animal model.

The specification fails to provide any guidance for successfully treating human patients with Alzheimer's disease, other amyloidoses or kidney failure and since resolution of the various complications in regards to treating these disorders with quinine or quinidine is not complete, one of skill in the art would be unable to practice the invention without engaging in undue trial and error experimentation. Additionally, a person skilled in the art would recognize that predicting the efficacy of quinine or

quinidine in humans in an Alzheimer's disease model as highly problematic (see MPEP §2164.03). Thus, although the specification prophetically considers using the claimed methods, such a disclosure would not be considered enabling since the state of the art teaches that treatment of Alzheimer's disease and associated diseases is highly unpredictable.

As set forth above, inadequate guidance is presented in the specification to overcome the obstacles outlined above in practicing the claimed invention. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the lack of working examples involving treatment of any patient with any disease (AD, amyloidoses, kidney failure or otherwise) comprising administration of quinine or quinidine, the lack of guidance present in the specification, the complex nature of the invention, and the prior art which establishes the complex nature of the claimed invention, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
13 July 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646